

RESPONSE

I. Restriction Requirement

The Examiner has determined that the original claims are directed to two separate and distinct inventions under 35 U.S.C. § 121, as follows:

- Group I: Claims 1-6, said to be drawn to an isolated nucleic acid encoding SEQ ID NO:2 including SEQ ID NO:1 and an isolated nucleic acid encoding SEQ ID NO:4 including SEQ ID NO:3, classified in class 536, subclass 23.5; and
- Group II: Claims 7 and 8, said to be drawn to a substantially isolated protein of SEQ ID NO:2 and variants thereof, classified in class 530, subclass 350.

II. Response to Restriction Requirement

In response to the Restriction Requirement, Applicants hereby confirm the election without traverse, made by Applicants' representative David Hibler during a telephone conference with the Examiner on May 5, 2003, to prosecute the claims of Group I invention (claims 1-6), drawn to an isolated nucleic acid encoding SEQ ID NO:2 including SEQ ID NO:1 and an isolated nucleic acid encoding SEQ ID NO:4 including SEQ ID NO:3, classified in class 536, subclass 23.5. Accordingly, claims 7 and 8 have been cancelled without prejudice and without disclaimer as being drawn to a non-elected invention.

Applicants reserve the right to refile claims to the non-elected invention in one or more future applications retaining the priority date of the present case and the earlier cited priority applications.

III. Status of the Claims

Claims 7 and 8 have been cancelled without prejudice and without disclaimer as being drawn to non-elected inventions. Claims 2 and 6 of the Group I invention have been cancelled without prejudice and without disclaimer. Claim 5 has been amended. New claims 9-13 have been added.

Claims 1, 3-5 and 9-13 are therefore presently pending in the case.

IV. Support for the Amended and Newly Added Claims

Claim 5 has been revised to correct the claim dependency, and to further clarify the claim. Support for this claim can be found throughout the specification as originally filed.

Claims 9-12 have been added to specifically recite expression vectors comprising nucleic acid

molecules of the present invention. Support for these claims can be found throughout the specification as originally filed, with particular support being found at least at page 16, lines 1-8.

Claim 13 has been added to specifically recite host cells comprising the expression vector of claim 9. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least at page 16, lines 9-15.

It will be understood that no new matter is included within the amended or newly added claims.

V. Objections

The Action first objects to claims 2 and 3 as being substantial duplicate claims. Applicants appreciate the guidance of the Examiner, and have cancelled claim 2 herein without prejudice and without disclaimer.

The Action next objects to claims 5 and 6 as being substantial duplicate claims. Applicants once again appreciate the guidance of the Examiner, and have cancelled claim 6 herein without prejudice and without disclaimer.

The Action next objects to claim 5 as being improperly dependent as it depends upon itself. Applicants apologize for the inadvertent clerical error, and have amended claim 5 to properly depend on claim 4.

The Action finally objects to claim 5 as grammatically incorrect, based on the term “wherein nucleotide sequence”. Applicants apologize for the inadvertent clerical error, and have amended claim 5 to recite “wherein said nucleotide sequence”.

As the present objections have been overcome, Applicants respectfully request that the objections be withdrawn.

VI. Rejection of Claims 2 and 5 Under 35 U.S.C. § 112, Second Paragraph

The Action next rejects claim 2 and 5 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the invention.

The Action rejects claim 2 as allegedly indefinite based on the fact that SEQ ID NO:3 is not an exact subsequence of SEQ ID NO:1. Applicants have therefore cancelled claim 2 without prejudice and without disclaimer. Applicants therefore respectfully request withdrawal of this rejection.

The Action also rejects claim 5 as allegedly indefinite, however, no details concerning this rejection are set forth in the Action. It appears that the rejection is based on the reasoning above, that

since SEQ ID NO:3 is not an exact subsequence of SEQ ID NO:1, that SEQ ID NO:4 would not be an exact subsequence of SEQ ID NO:2. However, SEQ ID NO:4 is in fact an exact subsequence of SEQ ID NO:2, since the mutation in SEQ ID NO:3 that is different from SEQ ID NO:1 merely introduces a stop codon, which is not reflected in the amino acid sequence of SEQ ID NO:4. Applicants therefore respectfully submit that the rejection of claim 5 under 35 U.S.C. § 112, second paragraph, is misplaced, and therefore request withdrawal of this rejection.

VII. Rejection of Claims 1-6 Under 35 U.S.C. § 101

The Action first rejects claims 1-6 under 35 U.S.C. § 101, as allegedly lacking a patentable utility. Applicants respectfully traverse.

The present invention has a number of substantial and credible utilities, not the least of which is in forensic biology, as described in the specification, at least at page 3, line 21. As described in the specification at page 19, lines 3-17, the present sequence defines a number of coding single nucleotide polymorphisms - specifically: a C/G polymorphism at nucleotide position 241 of SEQ ID NOS:1 and 3, which can result in an arg or gly at amino acid position 81 of SEQ ID NOS:2 and 4; a C/G polymorphism at nucleotide position 940 of SEQ ID NOS:1 and 3, which can result in a pro or ala at amino acid position 314 of SEQ ID NOS:2 and 4; a silent C/T polymorphism at nucleotide position 3465 of SEQ ID NOS:1 and 3, both of which result in an asp at amino acid position 1155 of SEQ ID NOS:2 and 4; and a silent C/T polymorphism at nucleotide position 5190 of SEQ ID NO:1, both of which result in a gly at amino acid position 1730 of SEQ ID NO:2. As such polymorphisms are the basis for forensic analysis, which is undoubtedly a “real world” utility, the present sequences must in themselves be useful. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Action states that this is not a specific utility for the claimed nucleic acids because “the specification fails to disclose a nexus between the claimed nucleic acid and a *specific* disease state” (Action at page 6, emphasis in original). Applicants respectfully point out that the use of the presently described polymorphisms in forensic analysis does not require the identification of a specific medical condition. Applicants respectfully point out that the presently described polymorphisms are useful in forensic analysis exactly as they were described in the specification as originally filed - specifically, to identify individual members of the human population based on the presence or absence of one or more of the described polymorphisms.

This is also not a case of a “potential” utility. Using the polymorphic markers exactly as

described in the specification as originally field can definitely distinguish members of a population from one another. In the worst case scenario, each marker is useful to distinguish 50% of the population (in other words, a marker being present in half of the population). The ability to eliminate 50% of the population from a forensic analysis clearly is a real world, practical utility. Therefore, any allegation that the use of the presently described polymorphic markers is only potentially useful would be without merit, and would not support the alleged lack of utility.

The Examiner states that “the asserted utilities are not specific to the claimed nucleic acids and are instead general utilities that would be applicable to the broad class of nucleic acids” (Action at page 6). This argument is flawed in a number of respects. First, not all nucleic acids contain polymorphic markers. In fact, the basis for forensic analysis is the fact that such polymorphic markers are not present in all other nucleic acids, but in fact specific and unique to only a certain subset of the population. Until a polymorphic marker is actually described it cannot be used in forensic analysis. Put another way, simply because there is a likelihood, even a significant likelihood, that a particular nucleic acid sequence will contain a polymorphism and thus be useful in forensic analysis, until such a polymorphism is actually identified and described, such a likelihood is meaningless. The Examiner appears to be attempting to use the information presented for the first time by Applicants in the instant specification as hindsight verification that the presently claimed sequence would be expected to have polymorphic markers. Such hindsight analysis based on Applicants discovery is completely improper. Second, the Examiner seems to be confusing the requirement for a specific utility, which is the proper standard for utility under 35 U.S.C. § 101, with the requirement for a unique utility, which is clearly an improper standard. As clearly set forth by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991):

An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: “[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility.” *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

Just because other, or even more useful, polymorphic sequences from the human genome have been described does not mean that the use of the presently described polymorphic markers for forensic analysis is not a specific utility. If every invention were required to have a unique utility, the Patent and Trademark Office would no longer be issuing patents on batteries, automobile tires, golf balls, golf clubs, and treatments for a variety of human diseases, such as cancer, just to name a few particular examples, because the utility of each of these compositions is applicable to the broad class in which

each of these compositions falls: all batteries have the same utility, specifically to provide electrical power; all automobile tires have the same utility, specifically for use on automobiles; all golf balls and golf clubs have the same utility, specifically for use in the game of golf; and all cancer treatments have the same utility, specifically, to treat cancer. However, only the briefest perusal of virtually any issue of the Official Gazette provides numerous examples of patents being granted on each of the above compositions nearly every week. Furthermore, if a composition needed to be unique to be patented, the entire class and subclass system would be an effort in futility, as the class and subclass system serves solely to group such common inventions, which would not be required if each invention needed to have a unique utility. Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

Furthermore, as the presently described polymorphisms are part of the family of polymorphisms that have a well established utility, the Federal Circuit's holding in *In re Brana*, (34 USPQ2d 1436 (Fed. Cir. 1995), "*Brana*") is directly on point. In *Brana*, the Federal Circuit admonished the Patent and Trademark Office for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. The Federal Circuit went on to state:

At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under 35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted, emphasis added. As set forth above, the present

polymorphisms are useful in forensic analysis exactly as they were described in the specification as originally filed, without the need for any further research. Even if the use of these polymorphic markers provided additional information on the percentage of particular subpopulations that contain these polymorphic markers, this would not mean that “additional research” is needed in order for these markers as they are presently described in the instant specification to be of use to forensic science. As stated above, using the polymorphic markers as described in the specification as originally filed can definitely distinguish members of a population from one another. However, even if, *arguendo*, further research might be required in certain aspects of the present invention, this does not preclude a finding that the invention has utility, as set forth by the Federal Circuit’s holding in *Brana*, which clearly states, as highlighted in the quote above, that “pharmaceutical inventions, necessarily includes the expectation of further research and development” (*Brana* at 1442-1443, emphasis added). In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is “undue”, not “experimentation”. *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra; Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988).

It is important to note that it has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have reason to doubt the objective truth of such statement. *In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA, 1974; “*Langer*”); *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA, 1971). As clearly set forth in *Langer*:

As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope.

Langer at 297, emphasis in original. As set forth in the MPEP, “Office personnel must provide evidence sufficient to show that the statement of asserted utility would be considered ‘false’ by a person of ordinary skill in the art” (MPEP, Eighth Edition at 2100-40, emphasis added). Absent such evidence from the Examiner, as the skilled artisan would readily understand that the present polymorphic markers

have utility in forensic analysis, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Examiner points out in the Action that the presently claimed sequence shares greater than 96% identity with two sequences that are present in the leading scientific repository for biological sequence data (GenBank), and have been annotated by independent third party scientists *wholly unaffiliated with Applicants* as Ten-m4 (GenBank Accession Number AB025413; alignment and GenBank report provided in **Exhibit A**), and DOC4 (GenBank Accession Number AF059485; alignment and GenBank report provided in **Exhibit B**). Additionally, the presently claimed sequence also shares greater than 96% identity with a sequence that has also been annotated by a third group of independent third party scientists *wholly unaffiliated with Applicants* as Ten-m4 (GenBank Accession Number NM_011858; alignment and GenBank report provided in **Exhibit C**). The legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. Given all of these GenBank annotations, there can be no question that those skilled in the art would clearly believe that Applicants' sequence is a human Ten-m4 variant, exactly as asserted by Applicants (see at least, the title of the application). Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

The Examiner cites Brenner (*Trends Genet.* **15**:132-133, 1999) and Scott *et al.* (*Nat. Genet.* **21**:440-443, 1999) to support the allegation that “functional assignment based on sequence similarity or identity alone, particularly in the instant case where the homologous sequences share a relatively low sequence identity, can lead to erroneous functional assignment” (Action at page 7). However, as clearly shown above, in the present case the homologous sequences (ten-m4 proteins) share an extremely high sequence identity (greater than 96% identical over the entire length of the protein). Thus, the present situation appears to track Example 10 of the Revised Interim Utility Guidelines Training Materials (pages 53-55; **Exhibit D**), which clearly establishes that a rejection under 35 U.S.C. § 101 as allegedly lacking a patentable utility and under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility (see Section VIII, below), is not proper when a full length sequence (such as the presently claimed sequence), and has a similarity score greater than 95% to a protein having a known function. Therefore, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

Given the well-established involvement of ten-m proteins in development (see, for example, Feng *et al.*, *J. Biol. Chem.* **277**:26128-26135, 2002; **Exhibit E**, as well as Oohashi *et al.*, *J. Cell Biol.* **145**:563-577, 1999, which was cited by the Examiner in the Action), as an additional example

of the utility of the present nucleotide sequences, the skilled artisan would readily appreciate the utility of tracking expression of the presently claimed sequence. The specification details, at least at page 6, lines 24-27, that the present nucleotide sequences have utility in assessing gene expression patterns using high-throughput DNA chips. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, 5,837,832, 6,156,501 and 6,261,776. As the present sequences are specific markers of human chromosome 11 (see below), those of skill in the art would instantly recognize that the present nucleotide sequences would be an ideal, novel candidate for assessing gene expression using such DNA chips. Given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* sequences would have great utility in such DNA chip applications. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequences, must in themselves be useful.

Evidence of the "real world" substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, one such company (Rosetta Inpharmatics) was viewed to have such "real world" value that it was acquired by large a pharmaceutical company (Merck) for significant sums of money (net equity value of the transaction was \$620 million). The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, persons of skill in the art, as well as venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. Billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, 2001, *Science* 291:1304). The results have been a stunning success as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, *Science* 291:1153). Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years). Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

The Examiner also questions this asserted utility, stating that the utility is “not specific as virtually *any* nucleic acid has utility” in such applications (Action at page 6, emphasis in original). This argument is also flawed in at least two respects. First, Applicants submit that only expressed sequences can be used to track gene expression, not just any nucleic acid. Expression profiling does not require a knowledge of the function of the particular nucleic acid on the chip - rather the gene chip indicates which DNA fragments are expressed at greater or lesser levels in two or more particular tissue types. Skilled artisans already have used and continue to use sequences such as Applicants in gene chip applications without further experimentation. Second, the Examiner again seems to be confusing the requirements of a specific utility with a unique utility. The fact that other nucleotide sequences can be used to track gene expression does not mean that the use of Applicants’ sequence to track gene expression is not a specific utility (*Carl Zeiss Stiftung v. Renishaw PLC, supra*). Therefore, this argument completely fails to support the alleged lack of utility of the presently claimed compositions.

Although Applicants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), as a further example of the utility of the presently claimed polynucleotide, as described in the specification at least at page 3, lines 12-15, the present nucleotide sequence has a specific utility in “identification of coding sequence” and “mapping a unique gene to a particular chromosome”. In fact, alignment of the presently claimed sequences with GenBank accession numbers AP002768, AP002957 and AP002515 (three overlapping clones from human chromosome 11) shows that the human gene corresponding to the presently claimed sequence is dispersed on 28 exons of human chromosome 11 (alignments and first pages of GenBank reports are presented in **Exhibit F**). Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of human chromosome 11 that contains the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence. For further evidence in support of the Applicants’ position, the Examiner is requested to review, for example,

section 3 of Venter *et al.* (*supra*, at pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Action once again states that “virtually *any* nucleic acid has utility” in such applications (Action at page 6, emphasis in original). First, Applicants respectfully remind the Examiner that only a minor percentage (2-4%) of the genome actually encodes exons, which in-turn encode amino acid sequences. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). As described in the specification as originally filed at page 3, lines 15-18, the claimed sequences “identify biologically verified exon splice junctions, as opposed to splice junctions that may have been bioinformatically predicted from genomic sequence alone”. The specification also details that “sequences derived from regions adjacent to the intron/exon boundaries of the human gene can be used to design primers for use in amplification assays to detect mutations within the exons, introns, splice sites (*e.g.*, splice acceptor and/or donor sites), *etc.*, that can be used in diagnostics and pharmacogenomics” (specification at page 12, lines 22-27). Applicants respectfully submit that the practical scientific value of biologically validated, expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. Second, the Examiner again seems to be confusing the requirements of a specific utility with a unique utility. The fact that other nucleotide sequences can be used to identify exon splice junctions and map human chromosome 11 does not mean that these uses of Applicants’ sequence are not specific utilities (*Carl Zeiss Stiftung v. Renishaw PLC, supra*). Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

Rather, as set forth by the Federal Circuit, “(t)he threshold of utility is not high: An invention is ‘useful’ under section 101 if it is capable of providing some identifiable benefit.” *Juicy Whip Inc. v. Orange Bang Inc.*, 51 USPQ2d 1700 (Fed. Cir. 1999) (citing *Brenner v. Manson*, 383 U.S. 519, 534 (1966)). Additionally, the Federal Circuit has stated that “(t)o violate § 101 the claimed device must be totally incapable of achieving a useful result.” *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 (Fed. Cir. 1992), emphasis added. *Cross v. Iizuka* (224 USPQ 739 (Fed. Cir. 1985); “*Cross*”) states “any utility of the claimed compounds is sufficient to satisfy 35 U.S.C.

§ 101". *Cross* at 748, emphasis added. Indeed, the Federal Circuit recently emphatically confirmed that "anything under the sun that is made by man" is patentable (*State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 47 USPQ2d 1596, 1600 (Fed. Cir. 1998), citing the U.S. Supreme Court's decision in *Diamond vs. Chakrabarty*, 206 USPQ 193 (S.Ct. 1980)).

Finally, the requirements set forth in the Action for compliance with 35 U.S.C. § 101 do not comply with the requirements set forth by the Patent and Trademark Office ("the PTO") itself for compliance with 35 U.S.C. § 101. While Applicants are well aware of the new Utility Guidelines set forth by the USPTO, Applicants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Applicants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines. As examples of such issued U.S. Patents, the Examiner is invited to review U.S. Patent Nos. 5,817,479, 5,654,173, and 5,552,281 (each of which claims short polynucleotides), and recently issued U.S. Patent No. 6,340,583 (which includes no working examples), none of which contain examples of the "real-world" utilities that the Examiner seems to be requiring. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section VIII, below), Applicants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Applicants understand that each application is examined on its own merits, Applicants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. Thus, holding Applicants to a different standard of utility would be arbitrary and capricious, and, like other clear violations of due process, cannot stand.

For each of the foregoing reasons, Applicants submit that as the presently claimed nucleic acid molecules have been shown to have a substantial, specific, credible and well-established utility, the

rejection of claims 1-6 under 35 U.S.C. § 101 has been overcome, and request that the rejection be withdrawn.

VIII. Rejection of Claims 1-6 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claims 1-6 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse.

Applicants submit that as claims 1-6 have been shown to have “a specific, substantial, and credible utility”, as detailed in section VII above, the present rejection of claims 1-6 under 35 U.S.C. § 112, first paragraph, cannot stand.

Applicants therefore request that the rejection of claims 1-6 under 35 U.S.C. § 112, first paragraph, be withdrawn.

IX. Rejection of Claim 4 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claim 4 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse.

35 U.S.C. § 112, first paragraph, requires that the specification contain a written description of the invention. The Federal Circuit in *Vas-Cath Inc. v. Mahurkar* (19 USPQ2d 1111 (Fed. Cir. 1991); “*Vas-Cath*”) held that an “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*.” *Vas-Cath*, at 1117, emphasis in original. However, it is important to note that the above finding uses the terms reasonable clarity to those skilled in the art. Further, the Federal Circuit in *In re Gosteli* (10 USPQ2d 1614 (Fed. Cir. 1989); “*Gosteli*”) held:

Although [the applicant] does not have to describe exactly the subject matter claimed, . . . the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.

Gosteli at 1618, emphasis added. Additionally, *Utter v. Hiraga* (6 USPQ2d 1709 (Fed. Cir. 1988); “*Utter*”), held “(a) specification may, within the meaning of 35 U.S.C. § 112 ¶1, contain a written description of a broadly claimed invention without describing all species that claim encompasses”

(*Utter*, at 1714). Therefore, all Applicants must do to comply with 35 U.S.C. § 112, first paragraph, is to convey the invention with reasonable clarity to the skilled artisan.

Further, the Federal Circuit has held that an adequate description of a chemical genus “requires a precise definition, such as by structure, formula, chemical name or physical properties” sufficient to distinguish the genus from other materials. *Fiers v. Sugano*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993; “*Fiers*”). *Fiers* goes on to hold that the “application satisfies the written description requirement since it sets forth the . . . nucleotide sequence” (*Fiers* at 1607). In other words, provision of a structure and formula - the nucleotide sequence - renders the application in compliance with 35 U.S.C. § 112, first paragraph.

More recently, the standard for complying with the written description requirement in claims involving chemical materials has been explicitly set forth by the Federal Circuit:

In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. *Regents of Univ. of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Thus, a claim describing a genus of nucleic acids by structure, formula, chemical name or physical properties sufficient to allow one of ordinary skill in the art to distinguish the genus from other materials meets the written description requirement of 35 U.S.C. § 112, first paragraph. As further elaborated by the Federal Circuit in *Regents of Univ. of California v. Eli Lilly and Co.*:

In claims to genetic material ... a generic statement such as ‘vertebrate insulin cDNA’ or ‘mammalian insulin cDNA’, without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art cannot, as one can do with a fully described genus, visualize or recognize the identity of members of the genus. (Emphasis added)

Thus, as opposed to the situation set forth in *Regents of Univ. of California v. Eli Lilly and Co.* and *Fiers*, the nucleic acid sequences of the present invention are not distinguished on the basis of function, or a method of isolation, but in fact are distinguished by structural features - a chemical formula, *i.e.*, the *sequence itself*.

Using the nucleic acid and amino acid sequences of the present invention (as set forth in the Sequence Listing), the skilled artisan would readily be able to distinguish the claimed nucleic acids from

other materials on the basis of the specific structural description provided. Polynucleotides that encode SEQ ID NO:4 are within the genus of the instant claims, while those that lack this structural feature lie outside the genus. Claim 4 thus meets the written description requirement.

Applicants note for the record that the Examiner's comments concerning the scope of claims 1 and 4, as set forth on page 10 of the Action, are not only directly in contrast with the relevant case law concerning the requirements under 35 U.S.C. § 112, first paragraph, as set forth in detail above, but are also contradicted by the wealth of case law concerning claim scope. Applicants assert for the record that the scope of claims 1 and 4 are not limited in any way by the Examiner's erroneous comments, and should be given their fullest possible scope.

For each of the foregoing reasons, Applicants submit that the rejection of claim 4 under 35 U.S.C. § 112, first paragraph, has been overcome, and request that the rejection be withdrawn.

X. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Steadman have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

October 9, 2003

Date



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